

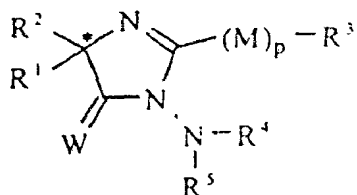


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FUNGICIDAL OPTICALLY ACTIVE 2-IMIDAZOLIN-5-ONE AND 2-IMIDAZOLINE-5-THIONE DERIVATIVES
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- (56) Prior Art Documents
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 EP 303863
- (57) Claim

1. Optically active 2-imidazolin-5-one or 2-imidazoline-5-thione derivatives of general formula I,



in which:

- W represents an oxygen or sulphur atom or an S=O group;
- M represents an oxygen or sulphur atom, or an optionally halogenated CH₂ radical;
- p is an integer equal to 0 or 1;
- * means the asymmetric carbon atom corresponding to a stereospecific

configuration and that the optically active derivative is substantially free from the other isomer;

-R¹ and R² are different and represent:

- an alkyl or haloalkyl radical containing 1 to 6 carbon atoms or
- an alkoxyalkyl, alkylthioalkyl, alkylsulphonylalkyl, monoalkylaminoalkyl, alkenyl or alkynyl radical containing 2 to 6 carbon atoms or

- a dialkylaminoalkyl or cycloalkyl radical containing 3 to 7 carbon atoms or

- an aryl^{or heteroaryl} radical comprising phenyl, naphthyl, thienyl, furyl, pyridyl, benzothienyl, benzofuryl, quinolyl, isoquinolyl or methylenedioxyphenyl, optionally substituted by 1 to 3 groups chosen from R⁶ or

- an arylalkyl, aryloxyalkyl, arylthioalkyl or arylsulphonylalkyl radical, the terms aryl and alkyl having the definitions given above or

- R¹ and R² can form, with the carbon to which they are bonded on the ring, a carbocycle or a heterocycle having from 5 to 7 atoms, it being possible for these rings to be fused to a phenyl, optionally substituted by 1 to 3 groups

chosen from R⁶;

- R³ represents:

- a hydrogen or an optionally halogenated C₁-C₂ alkyl radical, when p is equal to 0 or (M)_p is a CH₂ radical,
- an optionally halogenated C₁-C₂ alkyl radical, when (M)_p represents an oxygen or sulphur atom;

-R⁴ represents:

- the hydrogen atom or
- an alkyl group containing 1 to 6 carbon atoms or
- an alkoxyalkyl, alkylthioalkyl, haloalkyl, cyanoalkyl, thiocyanatoalkyl, alkenyl or alkynyl group containing 2 to 6 carbon atoms or
- a dialkylaminoalkyl, alkoxycarbonylalkyl or N-alkylcarbamoylealkyl group containing 3 to 6 carbon atoms or
- an N,N-dialkylcarbamoylealkyl group containing 4 to 8 carbon atoms or
- an aryl^{or heteroaryl} radical, comprising phenyl, naphthyl, thienyl, furyl, pyridyl, pyrimidinyl, pyridazinyl, pyrazinyl, benzothienyl, benzofuryl, quinolyl, isoquinolyl or methylenedioxyphenyl, optionally substituted by 1 to 3 groups chosen from R⁶ or
- an arylalkyl, aryloxyalkyl,

arylthioalkyl or arylsulphonylalkyl radical, the terms aryl and alkyl having the definitions given above;

-R⁵ represents:

- H, except when R⁴ is H, or
- an alkyl, haloalkyl, alkylsulphonyl or haloalkylsulphonyl radical containing 1 to 6 carbon atoms or
- an alkoxyalkyl, alkylthioalkyl, acyl, alkenyl, alkynyl, haloacyl, alkoxycarbonyl, haloalkoxycarbonyl, alkoxyalkylsulphonyl or cyanoalkylsulphonyl radical containing 2 to 6 carbon atoms or
- an alkoxyalkoxycarbonyl, alkylthioalkoxycarbonyl or cyanoalkoxycarbonyl radical containing 3 to 6 carbon atoms or
- the formyl radical or
- a cycloalkyl, alkoxyacyl, alkylthioacyl, cyanoacyl, alkenylcarbonyl or alkynylcarbonyl radical containing 3 to 6 carbon atoms or
- a cycloalkylcarbonyl radical containing 4 to 8 carbon atoms or
- a phenyl; arylalkylcarbonyl, especially phenylacetyl and phenylpropionyl; arylcarbonyl, especially benzoyl, optionally

substituted by 1 to 3 groups from R⁶;
thienylcarbonyl; furylcarbonyl;
pyridylcarbonyl; benzyloxycarbonyl;
furfuryloxycarbonyl;
tetrahydrofurfuryloxycarbonyl;
thienylmethoxycarbonyl;
pyridylmethoxycarbonyl; phenoxycarbonyl
or (phenylthio)carbonyl, the phenyl
being itself optionally substituted by 1
to 3 groups from R⁶; (alkylthio)carbonyl;
(haloalkylthio)carbonyl;
(alkoxyalkylthio)carbonyl;
(cyanoalkylthio)carbonyl;
(benzylthio)carbonyl;
(furfurylthio)carbonyl;
(tetrahydrofurfurylthio)carbonyl;
(thienylmethylthio)carbonyl;
(pyridylmethylthio)carbonyl or
arylsulphonyl radical or
- a carbamoyl radical, optionally mono-
or disubstituted by:

- an alkyl or haloalkyl group
containing 1 to 6 carbon atoms or
- a cycloalkyl, alkenyl or alkynyl
group containing 3 to 6 carbon
atoms or
- an alkoxyalkyl, alkylthioalkyl or
cyanoalkyl group containing 2 to 6
carbon atoms or
- a phenyl, optionally substituted

- by 1 to 3 R^6 groups;
- a sulphamoyl group, optionally mono- or disubstituted by:
 - an alkyl or haloalkyl group containing 1 to 6 carbon atoms or
 - a cycloalkyl, alkenyl or alkynyl group containing 3 to 6 carbon atoms or
 - an alkoxyalkyl, alkylthioalkyl or cyanoalkyl group containing 2 to 6 carbon atoms or
 - a phenyl, optionally substituted by 1 to 3 R^6 groups;
 - an alkylthioalkylsulphonyl group containing 3 to 8 carbon atoms or a cycloalkylsulphonyl group containing 3 to 7 carbon atoms;
 - R^4 and R^5 , taken together, can also form, with the nitrogen atom to which they are attached, a pyrrolidino, piperidino, morpholino or piperazino, optionally substituted by an alkyl containing 1 to 3 carbon atoms, group;
- R^6 represents:
- a halogen atom or
 - an alkyl, haloalkyl, alkoxy, haloalkoxy, alkylthio, haloalkylthio or alkylsulphonyl radical containing 1 to 6 carbon atoms or
 - a cycloalkyl, halocycloalkyl,

alkenyloxy, alkynyloxy, alkenylthio or
alkynylthio radical containing 3 to 6

carbon atoms or

- the nitro or cyano group or

- an amino radical, optionally mono- or
disubstituted by an alkyl or acyl

radical containing 1 to 6 carbon atoms

or an alkoxycarbonyl radical containing
2 to 6 carbon atoms

- a phenyl, phenoxy or pyridyloxy

radical, these radicals optionally being

substituted by 1 to 3 groups, which are

identical or different, chosen from R^7 ;

- R^7 represents:

- a halogen atom chosen from fluorine,
chlorine, bromine or iodine, or

- a linear or branched alkyl radical
containing from 1 to 6 carbon atoms, or

- a linear or branched alkoxy or
alkylthio radical containing from 1 to
6 carbon atoms, or

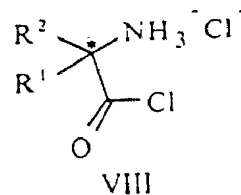
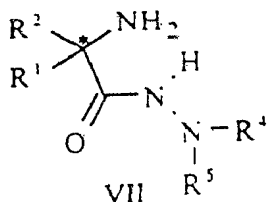
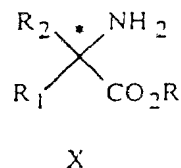
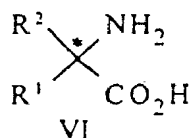
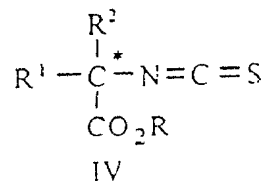
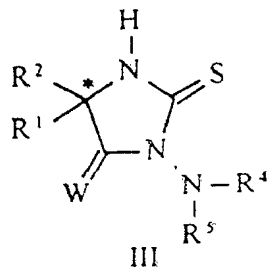
- a linear or branched haloalkoxy or
haloalkylthio radical containing from 1
to 6 carbon atoms, or

- a nitrile radical, or

- a nitro radical;

and the agriculturally-acceptable salified forms of
these compounds.

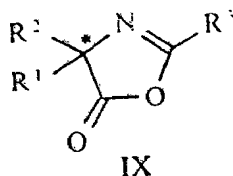
13. Optically active compounds which are useful especially as intermediates in the preparation of the compounds of formula I according to one of claims 1 to 4, characterized in that they have the formula:



in which R represents a C₁-C₄ alkyl wherein * means the asymmetric carbon atom corresponding to a stereospecific configuration and that the optionally active compound is substantially free from the other isomer, and R¹ to R⁵ have the same meanings as in

the general formula I of the invention,

and of formula IX:

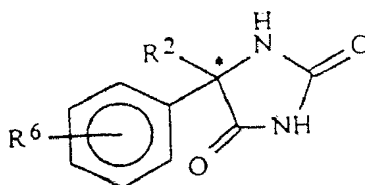


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in which * has the same meaning as above, R^3 represents an optionally halogenated C_1-C_3 alkyl radical,

and of formula XIIb:



XIIb

in which * has the same meaning as above, R^2 has the same meaning as above and R^6 represents a phenyl, phenoxy or pyridyloxy radical, these radicals optionally being substituted by 1 to 3 groups, which are identical or different, chosen from R^7 as defined above.

16. Process for the treatment of crops affected by or capable of being affected by fungal diseases, characterized in that an effective amount of an optically active compound of formula I according to one of claims 1 to 4 is applied preventively or curatively.

AUSTRALIA
PATENTS ACT 1990
COMPLETE SPECIFICATION

NAME OF APPLICANT(S):

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INVENTION TITLE:

Fungicidal optically active 2-imidazolin-5-one and 2-imidazoline-5-thione derivatives

The following statement is a full description of this invention, including the best method of performing it known to me/us:-

The subject of the present invention is new optically active 2-imidazolin-5-one and 2-imidazoline-5-thione derivatives for use in plant protection, their process of preparation and the compounds which can optionally be used as intermediates in the preparation processes. It also relates to fungicidal compositions based on these compounds and to a process for the treatment of fungal diseases of crops using these compounds.

The racemic compounds derived from 2-imidazolin-5-ones and 2-imidazoline-5-thiones are described in European Patent Applications EP 551048 and EP 599749, and in International Application WO 94/01410.

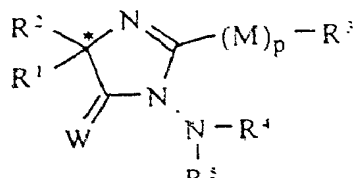
It has now been discovered that one of the optical isomers of these compounds has a biological activity which is much greater than that of the other isomer and that of the racemic modification.

One object of the invention is therefore to provide new compounds which are useful in controlling fungal diseases of crops.

Another object of the invention is to provide new 2-imidazolin-5-one and 2-imidazoline-5-thione derivatives which are active at a dose which is reduced with respect to that of the racemic derivatives.

It has now been found that these objects could be achieved by virtue of the products of the

invention, which are optically active 2-imidazolin-5-one or 2-imidazoline-5-thione derivatives of general formula I:



in which:

-W represents an oxygen or sulphur atom or an S=O group;

5 -M represents an oxygen or sulphur atom, or an optionally halogenated CH₂ radical;

-p is an integer equal to 0 or 1;

* means the asymmetric carbon atom corresponding to a stereospecific.

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configuration and that the optically active derivative is substantially free from the other isomer;

-R¹ and R² are different and represent:

15

- an alkyl or haloalkyl radical containing 1 to 6 carbon atoms or
- an alkoxyalkyl, alkylthioalkyl, alkylsulphonylalkyl, monoalkylaminoalkyl, alkenyl or alkynyl radical containing 2 to 6 carbon atoms or

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- a dialkylaminoalkyl or cycloalkyl radical containing 3 to 7 carbon atoms or



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or heteroary³
 - an aryl radical comprising phenyl,
 naphthyl, thienyl, furyl, pyridyl,
 benzothienyl, benzofuryl, quinolyl,
 isoquinolyl or methylenedioxyphenyl,
 optionally substituted by 1 to 3 groups
 chosen from R⁶ or

10

- an arylalkyl, aryloxyalkyl,
 arylthioalkyl or arylsulphonylalkyl
 radical, the terms aryl and alkyl having
 the definitions given above or

15

- R¹ and R² can form, with the carbon to
 which they are bonded on the ring, a
 carbocycle or a heterocycle having from
 5 to 7 atoms, it being possible for
 these rings to be fused to a phenyl,
 optionally substituted by 1 to 3 groups
 chosen from R⁶;

20

- R³ represents:
 - a hydrogen or an optionally
 halogenated C₁-C₃ alkyl radical, when p
 is equal to 0 or (M)_p is a CH₂ radical,
 - an optionally halogenated C₁-C₃ alkyl
 radical, when (M)_p represents an oxygen
 or sulphur atom;

25

- R⁴ represents:
 - the hydrogen atom or
 - an alkyl group containing 1 to 6
 carbon atoms or



- an alkoxyalkyl, alkylthioalkyl, haloalkyl, cyanoalkyl, thiocyanatoalkyl, alkenyl or alkynyl group containing 2 to 6 carbon atoms or

5

- a dialkylaminoalkyl, alkoxycarbonylalkyl or N-alkylcarbamoylealkyl group containing 3 to 6 carbon atoms or

- an N,N-dialkylcarbamoylealkyl group containing 4 to 8 carbon atoms or

10

- an aryl^{or heteroaryl} radical, comprising phenyl, naphthyl, thienyl, furyl, pyridyl,

pyrimidinyl, pyridazinyl, pyrazinyl, benzothienyl, benzofuryl, quinolyl,

15

isoquinolyl or methylenedioxyphenyl, optionally substituted by 1 to 3 groups chosen from R⁶ or

- an arylalkyl, aryloxyalkyl,

arylthioalkyl or arylsulphonylalkyl

20

radical, the terms aryl and alkyl having the definitions given above;

-R⁵ represents:

- H, except when R⁴ is H, or

25

- an alkyl, haloalkyl, alkylsulphonyl or haloalkylsulphonyl radical containing 1 to 6 carbon atoms or

- an alkoxyalkyl, alkylthioalkyl, acyl, alkenyl, alkynyl, haloacyl,



- alkoxycarbonyl, haloalkoxycarbonyl,
alkoxyalkylsulphonyl or
cyanoalkylsulphonyl radical containing 2
to 6 carbon atoms or
- 5 - an alkoxyalkoxycarbonyl,
alkylthioalkoxycarbonyl or
cyanoalkoxycarbonyl radical containing 3
to 6 carbon atoms or
- 10 - the formyl radical or
- a cycloalkyl, alkoxyacyl,
alkylthioacyl, cyanoacyl,
alkenylcarbonyl or alkynylcarbonyl
radical containing 3 to 6 carbon atoms
or
- 15 - a cycloalkylcarbonyl radical
containing 4 to 8 carbon atoms or
- a phenyl; arylalkylcarbonyl,
especially phenylacetyl and
phenylpropionyl; arylcarbonyl,
especially benzoyl, optionally
- 20 substituted by 1 to 3 groups from R⁶;
thienylcarbonyl; furylcarbonyl;
pyridylcarbonyl; benzyloxycarbonyl;
furfuryloxycarbonyl;
- 25 tetrahydrofurfuryloxycarbonyl;
thienylmethoxycarbonyl;
pyridylmethoxycarbonyl; phenoxycarbonyl
or (phenylthio)carbonyl, the phenyl

being itself optionally substituted by 1
to 3 groups from R⁶; (alkylthio)carbonyl;
(haloalkylthio)carbonyl;
(alkoxyalkylthio)carbonyl;
(cyanoalkylthio)carbonyl;
(benzylthio)carbonyl;
(furfurylthio)carbonyl;
(tetrahydrofurfurylthio)carbonyl;
(thienylmethylthio)carbonyl;
(pyridylmethylthio)carbonyl or
arylsulphonyl radical or
- a carbamoyl radical, optionally mono-
or disubstituted by:

- an alkyl or haloalkyl group
containing 1 to 6 carbon atoms or
- a cycloalkyl, alkenyl or alkynyl
group containing 3 to 6 carbon
atoms or

- an alkoxyalkyl, alkylthioalkyl or
cyanoalkyl group containing 2 to 6
carbon atoms or
- a phenyl, optionally substituted
by 1 to 3 R⁶ groups;

- a sulphamoyl group, optionally mono-
or disubstituted by:

- an alkyl or haloalkyl group
containing 1 to 6 carbon atoms or
- a cycloalkyl, alkenyl or alkynyl

group containing 3 to 6 carbon atoms or

- an alkoxyalkyl, alkylthioalkyl or cyanoalkyl group containing 2 to 6 carbon atoms or

- a phenyl, optionally substituted by 1 to 3 R^6 groups;

- an alkylthioalkylsulphonyl group containing 3 to 8 carbon atoms or a cycloalkylsulphonyl group containing 3 to 7 carbon atoms;

- R^4 and R^5 , taken together, can also form, with the nitrogen atom to which they are attached, a pyrrolidino, piperidino, morpholino or piperazino, optionally substituted by an alkyl containing 1 to 3 carbon atoms, group;

$-R^6$ represents:

- a halogen atom or

- an alkyl, haloalkyl, alkoxy, haloalkoxy, alkylthio, haloalkylthio or alkylsulphonyl radical containing 1 to 6 carbon atoms or

- a cycloalkyl, halocycloalkyl, alkenyloxy, alkynyloxy, alkenylthio or alkynylthio radical containing 3 to 6 carbon atoms or

- the nitro or cyano group or

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- an amino radical, optionally mono- or disubstituted by an alkyl or acyl radical containing 1 to 6 carbon atoms or an alkoxycarbonyl radical containing 2 to 6 carbon atoms

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- a phenyl, phenoxy or pyridyloxy radical, these radicals optionally being substituted by 1 to 3 groups, which are identical or different, chosen from R⁷;
- R⁷ represents:

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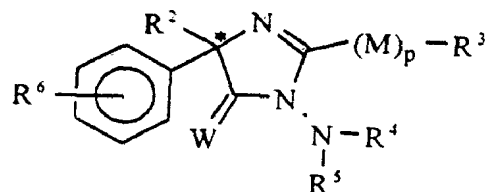
- a halogen atom chosen from fluorine, chlorine, bromine or iodine, or
- a linear or branched alkyl radical containing from 1 to 6 carbon atoms, or
- a linear or branched alkoxy or alkylthio radical containing from 1 to 6 carbon atoms, or
- a linear or branched haloalkoxy or haloalkylthio radical containing from 1 to 6 carbon atoms, or
- a nitrile radical, or
- a nitro radical.

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The invention also relates to the agriculturally-acceptable salified forms of the compounds defined above.

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According to a preferred variant of the invention, the optically active compounds according to the invention have the formula II:



in which the various symbols have the same meaning as in the formula I.

Finally, the compounds of the invention will advantageously be chosen from the compounds of formula II in which W represents an oxygen atom.

The method of preparation of the compounds of formula I is shown in the following paragraphs, according to two process variants A and B. The symbols represented in formula I, which appear in this description of the method of preparation, retain the same meaning as in the general definition of the invention, unless another definition is expressly attributed to them.

The examples below illustrate the optically active derivatives of formula I and their process of preparation.

The structures of all the derivatives illustrated were characterized using at least one of the following spectral techniques: proton NMR spectrometry, carbon-13 NMR spectrometry, infrared spectrometry and mass spectrometry, as well as the usual methods for measuring optical rotations. The enantiomeric excesses were determined either by chiral

phase high performance liquid chromatography or by NMR.

In the tables below, the phenyl, methyl and ethyl radicals are represented by Ph, Me and Et respectively.

5 Variant A:

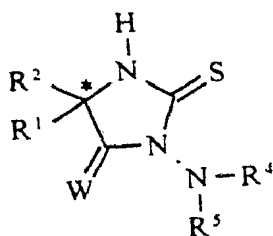
First stage:

 In a first stage of this variant, a description is given of the preparation of the optical isomers of formula I from α -amino acids which are
10 optically pure or greatly enriched in one enantiomer. Optically active compound greatly enriched in a specific enantiomer is understood to mean a compound containing at least 80 %, preferably 95 %, of this enantiomer.

15 The optical isomers of formula I are prepared according to three series of processes, depending on the meaning of the $(M)_p-R^3$ group.

 1) Preparation of the compounds of formula I in which $p = 1$ and $M = S$ and $W = O$:

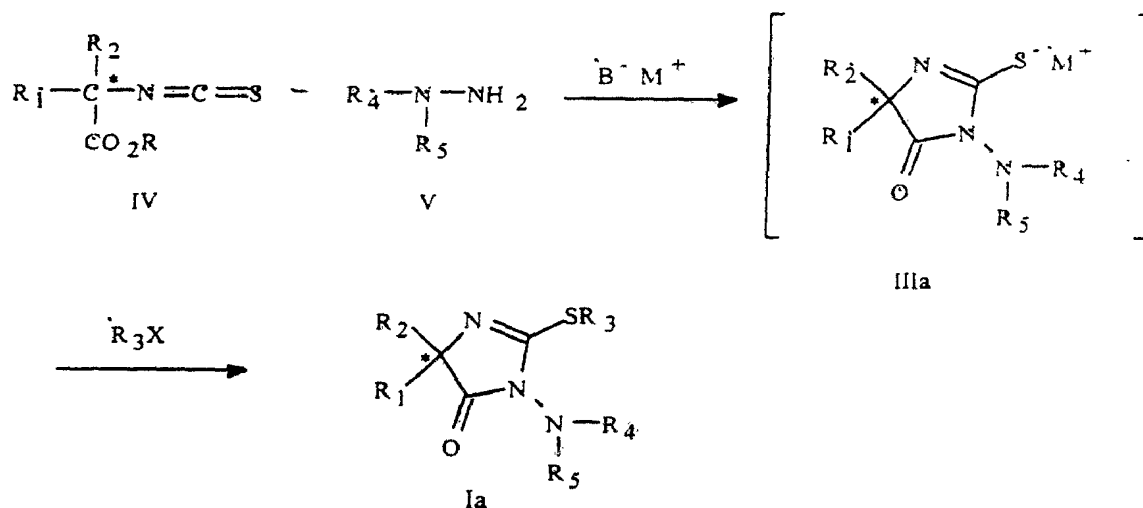
20 The compounds of formula I in which $p = 1$ and $M = S$ and $W = O$ are prepared by reaction of the compound of formula III:



in which W represents an oxygen atom, with the compound of formula R^3X , in which X represents the chlorine, bromine or iodine atom or the sulphate group or an alkylsulphonyloxy or arylsulphonyloxy group, alkyl and aryl being as defined above for R^1 and R^2 . The reaction is carried out in a solvent and in the presence of a base. It is possible to use, as base, an alkoxide, for example potassium tert-butoxide, an alkali metal or alkaline earth-metal hydroxide, an alkali metal carbonate or a tertiary amine. It is possible to use, as solvent, ethers, cyclic ethers, alkyl esters, acetonitrile, alcohols containing 1 to 3 carbon atoms or aromatic solvents, for example tetrahydrofuran, at a temperature between -5°C and $+80^\circ\text{C}$.

A variant of the method described above consists in using the so-called "one-pot" process (Diagram 1) as described in European Patent Application EP 551048. This method consists in starting directly from the isothiocyanate of formula IV which is treated with a compound of formula V in a solvent and in the presence of a base as described above. The intermediate

of formula IIIa in the salt form is not isolated but is treated directly with the compound of formula R^3X in which X has the same meaning as above



(Diagram 1)

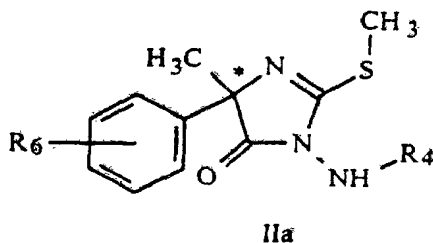
5 Example 1: (+)-(4S)-4-methyl-2-methylthio-4-phenyl-1-phenylamino-2-imidazolin-5-one (Compound No. 1)

682 g (3.08 mol) of methyl (+)-(2S)-2-phenyl-2-(isothiocyanato)propionate, dissolved in 4 l of anhydrous tetrahydrofuran, are introduced into a 20 l reactor through which passes a stream of argon. Cooling is carried out to 15°C. 343 g (3.08 mol) of phenylhydrazine, dissolved in 2 l of tetrahydrofuran, are run in over 30 min, the temperature being maintained between 15°C and 18°C. The mixture is kept stirring for 40 min and then cooled to 0°. A solution of 346 g (3.08 mol) of potassium tert-butoxide in 4 l of tetrahydrofuran is run in over 1 hour, the

temperature being maintained at 0°C. The mixture is stirred for a further 2 hours at 0°C and the formation of a pale-pink precipitate is observed. 218 ml (3.39 mol) of methyl iodide are run in over 15 min, the temperature being maintained between 0°C and 3°C, and the temperature is then allowed to rise to room temperature while continuing to stir for 2 hours. The reaction mixture is poured onto 5 l of water. After separating, the aqueous phase is extracted with 3 times 3 l of ethyl acetate. The combined organic phases are washed with 5 l of water, dried over magnesium sulphate and then concentrated under reduced pressure. 1099 g of a brown solid are obtained. The latter is recrystallized from 2 l of toluene.

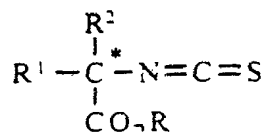
There are obtained, after drying, 555 g of (+)-(4S)-4-methyl-2-methylthio-4-phenyl-1-phenylamino-2-imidazolin-5-one in the form of an off-white solid melting at 138°C (Yield = 58 %; $[\alpha]_D^{27^\circ} = + 61.1^\circ$ (+ or - 2.9°) (c = 0.86 in ethanol); degree of enantiomeric excess (e.e) > 98 %).

In the same way, the following analogous compounds of formula IIa were obtained:

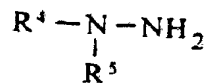


Compound No.	R ⁴	R ⁶	[α] _D (c) Solvent	M.p. (°C)	Yd (%)
1	Ph	H	+61° (0.8) EtOH	138	58
11	Ph	4-F	+53° (0.7) EtOH	114	60
12	Ph	4-F	(-)	114	66
13	3-FPh	4-F	+52° (0.7) EtOH	130	70
14	3-FPh	4-F	(-)	-	-
15	Ph	4-(4-FPh)O	(+)	138	45
16	Ph	4-(4-FPh)O	-13° (0.4) EtOH	139	71

The compound of formula III in which W represents an oxygen atom can be prepared by a cyclization reaction between an isothiocyanate of formula IV:



in which R represents a C₁-C₄ alkyl, and a compound of formula V:



The cyclization reaction can be carried out in two ways:

- thermally: in this case, the mixture of the reactants is heated at a temperature between 110°C and 180°C in an aromatic solvent such as toluene, xylene or chlorobenzenes,

5 - in basic medium: the cyclization reaction is carried out in the presence of one equivalent of a base such as an alkali metal alkoxide, an alkali metal hydroxide or a tertiary amine. Under these conditions, cyclization takes place at a temperature between -10
10 and +80°C. It is possible to use, as solvent, especially ethers, cyclic ethers, alcohols, esters, DMF or DMSO.

Example 2: (+)-(4S)-4-methyl-4-phenyl-1-phenylamino-2-thiohydantoin (Compound No. 7)

15 0.7 g (0.00316 mol) of methyl (+)-(2S)-2-isothiocyanato-2-phenylpropionate, diluted in 15 ml of dry tetrahydrofuran, is introduced into a 100 ml three-necked flask under a dry nitrogen atmosphere. 0.32 ml (0.00316 mol) of phenylhydrazine, diluted in 5
20 ml of tetrahydrofuran, is run in at 20°C in a single step. The temperature rises by 2°C. The medium is kept magnetically stirring for 30 min. Appearance of a dark-beige precipitate. The medium is neutralized with 0.4 ml of acetic acid and then treated with 20 ml of
25 water. After separating, the aqueous phase is extracted with 3 times 20 ml of ethyl ether. The organic phases are combined, washed with 2 times 30 ml of water, dried over magnesium sulphate and then concentrated under

reduced pressure. The solid residue obtained is chromatographed on a silica column, using an eluent mixture composed of heptane and ethyl acetate in the proportions 50/50.

- 5 0.55 g of (+)-(4S)-4-methyl-4-phenyl-1-phenylamino-2-thiohydantoin is collected in the form of a beige solid melting at 167°C (Yield = 58 %; $[\alpha]_{\text{D}}^{27^\circ\text{C}} = +86^\circ$ (+ or - 3.2°) (c = 0.8 in methanol)).

- 10 The isothiocyanates of formula IV can be prepared according to one of the processes mentioned in Sulfur Reports, Volume 8 (5), pages 327-375 (1989), from the α -amino acid of formula VI via the amino ester of formula X:



VI



X

- 15 in a way well known to those skilled in the art.

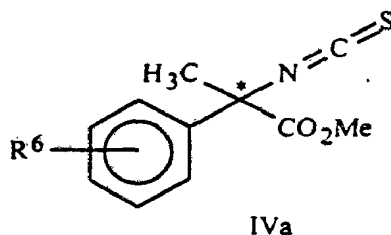
Example 3: methyl (+)-(2S)-2-isothiocyanato-2-phenylpropionate (Compound No. 8)

- 20 780 g (3.61 mol) of methyl (+)-(2S)-2-amino-2-phenylpropionate hydrochloride and then 3.4 l of water are introduced into a 20 l reactor. The temperature is brought to 20°C. 3.4 l of toluene are added and then 911 g (10.8 mol) of sodium

hydrogencarbonate are added portionwise over 1 hour. The temperature falls to 8-9°C. 276 ml (3.61 mol) of thiophosgene are run in over 2 hours. The reaction is accompanied by an evolution of gas and by a rise in temperature, which reaches 24°C at the end of the addition. The medium is kept stirring for a further 2 hours. After separating, the aqueous phase is extracted with 2 l of toluene. The combined toluene phases are washed with 4 l of water and then dried over magnesium sulphate. The solution is concentrated under reduced pressure.

There are obtained 682 g of methyl (+)-(2S)-2-isothiocyanato-2-phenylpropionate in the form of a slightly coloured oil (Yield = 85 %; $[\alpha]_D^{29^\circ} = +16^\circ$ (+ or - 6.4°) (c = 0.78 in chloroform)).

In the same way, the following analogous compounds of formula IVa were obtained:



Compound No.	R ⁶	[α] _D (c) Solvent	physical state	Yd (%)
8	H	+16° (0.78) CHCl ₃	Oil	85
17	4-F	(+)	Oil	72
18	4-F	(-)	Oil	80
19	4-(4-FPh)O	(+)	Oil	61
20	4-(4-FPh)O	-11° (0.7) EtOH	Oil	70

The amino esters of structure X can be obtained in a known way either by :

10 - diastereoselective amination of a prochiral compound followed by deprotection of the chiral moiety as described by R.S. Atkinson et al., Tetrahedron, 1992, 48, pp 7713-30,

15 - resolution of the corresponding racemate with a chiral compound as described by Y. Sugi and S. Mitsui, Bull. Chem. Soc. Japan, 1969, 42, pp 2984-89.

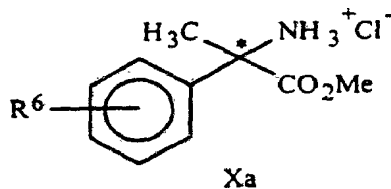
20 - esterification of a chiral amino acid as described by D.J. Cram et al., J. Am. Chem. Soc., 1961, 83, pp 2183-89.

Example 4: methyl (+)-(2S)-2-amino-2-phenylpropionate hydrochloride (Compound No. 9)

611 g (3.7 mol) of (+)-2-amino-phenylpropionic acid are charged to a 10 l reactor, to
25 which 5 l of methanol are added. 819 ml (11.22 mol) of

thionyl chloride are run onto the white suspension formed over 2 hours. The temperature reaches 58°C at the end of the addition. A significant evolution of gas is observed, which gas is trapped by a dilute sodium hydroxide solution. The medium is heated at 65°C for 14 hours. The solution is then concentrated under reduced pressure. The solid obtained is treated with 1 l of toluene, filtered and then dried under vacuum. There are obtained 762 g of methyl (+)-(2S)-2-amino-2-phenylpropionate hydrochloride in the form of a white powder melting at 162°C (Yield = 62 %; $[\alpha]_D^{25^\circ} = +53.3^\circ$ (+ or - 3.3°) (c = 0.75 in water)).

In the same way, the following analogous compounds of formula Xa were obtained:



Compound No.	R ⁶	[α] _D (c) Solvent	physical state	M.p. (°C)	Yd (%)
9	H	+54° (0.91) CHCl ₃	white crystals	162	62
21	4-F	+61° (0.9) EtOH	white solid	50-60	93
22	4-F	(-)	white solid	-	95
23	4-(4-FPh)O	(+)	white solid	-	87
24	4-(4-FPh)O	(-)	white solid	-	95

Methyl (+)-(2S)-2-amino-2-phenylpropionate is obtained by treating the hydrochloride prepared above with one equivalent of sodium hydrogencarbonate and then extracting with dichloromethane. It exists in the form of a colourless, slightly viscous oil ($[\alpha]_D^{29^\circ\text{C}} = +54.8^\circ$ (+ or - 2.7°) (c = 0.91 in chloroform), e.e > 95 %).

2) Preparation of the optical isomers of formula I in which p = 1 and M = O and W = O:

The compounds of formula I in which p = 1 and M = O and W = O are prepared by reacting the corresponding compound of formula I for which p = 1 and M = S, according to a process described in European Patent Application EP 599749, with the alcohol of formula R³OH, in a solvent, in the presence of a strong base and at a temperature between 50 and 80°C. It is

possible to use, as strong base, an alkali metal alkoxide $R^3O^-Met^+$, in which Met^+ represents an alkali metal or alkaline-earth metal, an alkali metal hydroxide or a strong organic base. The reaction is preferably carried out by taking the alcohol R^3OH as solvent and by using the corresponding sodium alkoxide $R^3O^-Na^+$ as base.

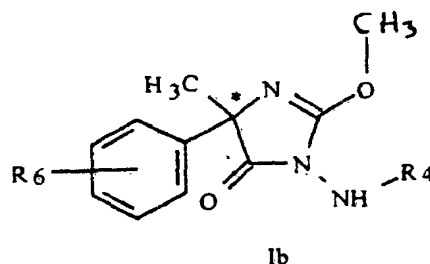
Example 5: (+)-(4S)-4-methyl-2-methoxy-4-phenyl-1-phenylamino-2-imidazolin-5-one (Compound No. 3)

80 ml of methanol and then 0.74 g (0.032 mol) of sodium, cut into thin pieces, are introduced into a 250 ml, three-necked, round-bottomed flask under a dry nitrogen atmosphere. 5 g (0.016 mol) of (+)-(4S)-4-methyl-2-methylthio-4-phenyl-1-phenylamino-2-imidazolin-5-one are then added. The mixture is brought to reflux for 20 h. The mixture is cooled to room temperature and then acidified with 0.5 ml of acetic acid. The methanol is removed by distillation under reduced pressure and the residue obtained is then taken up in 50 ml of ethyl ether, washed with 3 times 40 ml of water, dried over magnesium sulphate and then the solution is concentrated under reduced pressure. A reddish honey is obtained which is purified by chromatography on a silica column with a 70/30 heptane/ethyl acetate mixture as eluent.

2 g of (+)-(4S)-4-methyl-2-methoxy-4-phenyl-1-phenylamino-2-imidazolin-5-one are obtained in the form of a pale-pink powder melting at 132°C (Yield =

42%; $[\alpha]_D^{25^\circ} = +53.1^\circ$ (+ or - 2.4°) ($c = 1$ in methanol);
e.e. > 98 %).

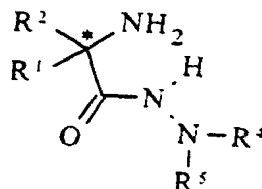
In the same way, the following analogous
compounds of formula Ib were obtained:



Compound No.	R^4	R^6	$[\alpha]_D$ (c) Solvent	M.p. ($^\circ\text{C}$)	Yd (%)
3	Ph	H	+53° (1.0) MeOH	132	42
25	Ph	4-F	+34° (0.5)	129	66
26	Ph	4-F	-33° (0.5) EtOH	129	66
27	3-FPh	4-F	+29° (0.5) EtOH	130	43
28	3-FPh	4-F	(-)	-	-
29	Ph	4-(4-FPh)O	(+)	glass	25
30	Ph	4-(4-FPh)O	-12° (0.4) EtOH	glass	44

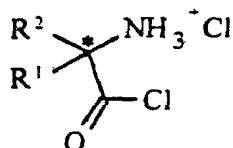
3) Preparation of the optical isomers of
formula I in which $p = 0$:

The compounds of formula I in which $p = 0$ and
 R^3 is a hydrogen atom are obtained from the compound of
formula VII:



by reacting the latter with dimethylformamide dimethyl acetal (DMFDMA). The reaction is carried out at a temperature between 10 and 100°C, in excess DMFDMA.

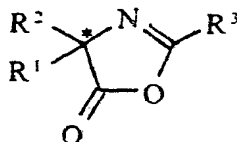
The compound of formula VII is prepared from
 5 a compound of formula VIII:



by reaction of the latter with the compound of formula V, at a temperature between -20 and 40°C, in a solvent consisting of a cyclic or non-cyclic ether, optionally in the presence of a base. The base is
 10 chosen from nitrogenous organic bases such as triethylamine or pyridine.

The compounds of formula VIII can be obtained from the α -amino acid of formula VI by observing the method described by S. Levine in J. Am. Chem. Soc. of
 15 1953, Volume 76, page 1392.

The optically active compounds of formula I in which R^3 is an optionally halogenated C_1-C_2 alkyl radical and in which $p = 0$ or $p = 1$ and $M = CH_2$ are obtained from the compound of formula IX:



5 in which R^3 represents a C_1-C_2 alkyl radical,
by reaction of the latter with the compound
of formula V, under conditions deduced, by analogy,
from the method set out in the article by J. P.
Branquet et al. in Bull. Soc. Chim. de France, 1965,
10 (10), pp 2942-2954.

This same article gives a procedure at the
end of which the compound of formula IX can be prepared
from the α -amino acid of formula VI.

Second stage:

15 The method of access to the optically pure or
greatly enriched α -amino acids of formula VI used in
the above stage is specified in this second stage.

These α -amino acids can be obtained according
to one of the following methods:

20 - either by diastereoselective synthesis and
then suppression of the chiral moiety, as described by
M. Chaari, A. Jenhi, J.P. Laverne and P. Viallefont in
Tetrahedron, 1991, Volume 4, pages 4619-4630,

- or by enzymatic resolution of the racemic

amide, for which method the following references may usefully be consulted:

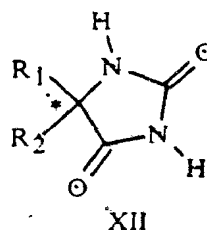
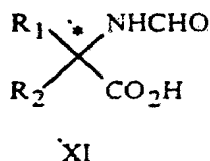
R.M. Kellog, E.M. Meijer et al., J. Org. Chem., 1988, Volume 53, pages 1826-1828

5 D. Rossi and A. Calcagni, Experimentia, 1985, volume 41, pages 35-37,

- or by hydrolysis of a chiral amino acid precursor such as, for example:

10 - a formyl amino acid of structure XI as described by MacKenzie and Clough, J. Chem. Soc., 1912, pp 390-397, or by D.J. Cram et al., J. Am. Chem. Soc., 1961, 83, pp 2183-89,

15 - a hydantoin of structure XII as described in published British Patent Application No. 1,201,168.



The compounds of formulae XI or XII can be obtained by resolution of the corresponding racemic modification with a chiral compound as described by MacKenzie and Clough, J. Chem. Soc., 1912, pp 390-397, 20 or by D.J. Cram et al., J. Am. Chem. Soc., 1961, 83, pp 2183-89, for the compound XI or as described in published International Patent Application No.

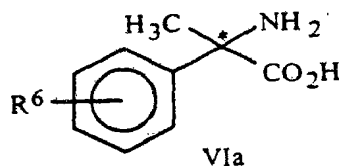
9,208,702 for the compound XII.

Example 6: (+)-(2S)-2-amino-2-phenylpropionic acid
(Compound No. 10)

22 g (0.115 mol) of (+)-(5S)-5-methyl-5-phenylhydantoin, 100 ml of water and 100 ml of 28% aqueous ammonia are introduced successively into a 1 litre autoclave. The medium is heated at 160°C for 15 hours. After cooling to room temperature, the solution is concentrated under reduced pressure. The white solid obtained is treated with 100 ml of ethyl acetate for 2 hours and then filtered and dried under vacuum at 80°C.

10.5 g of (+)-(2S)-2-amino-2-phenylpropionic acid are collected in the form of a white powder which has a decomposition temperature of 266°C (Yield = 55 %; $[\alpha]_D^{27^\circ} = +71.9^\circ$ (+ or - 3.1°) (c = 0.8 in 1N hydrochloric acid)).

In the same way, the following analogous compounds of formula VIa were obtained:



Compound No.	R ⁶	[α] _D (c) Solvent	M.p. (°C)	Yd (%)
10	H	+72° (0.8) 1N HCl	266	55
31	4-F	(+)	-	44
32	4-F	(-)	-	92
33	4-(4-FPh)O	(+)	-	87
34	4-(4-FPh)O	(-)	-	76

Example 9 illustrates the preparation of the compounds of formula XII

10 Example 9: (+)-(5S)-5-Methyl-5-phenylhydantoin
(Compound No. 35)

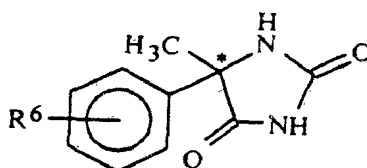
5.6 g (0.139 mol) of sodium hydroxide are added to a stirred suspension of 70.0 g (0.368 mol) of (5R,5S)-5-methyl-5-phenylhydantoin in 2000 ml of water.

15 The solution obtained is brought to 40°C and then 44.6 g (0.368 mol) of (+)-R- α -methylbenzylamine are added. The solution obtained is maintained at 50°C for 0.75 h and a white precipitate appears after 3 min. On completion of heating, the reaction medium is allowed
 20 to crystallize for 24 h, the crystals are then filtered, washed with 70 ml of water and pulled dry under an air stream for 2 h and there are recovered 45 g of a white solid which is added to 220 ml of 1N hydrochloric acid at 10°C. The suspension obtained is
 25 stirred for 2 h, the crystals are then filtered, washed with 100 ml of water and pulled dry and then dried

under reduced pressure at 50°C for 15 h. There are thus recovered 23 g (0.121 mol) of (+)-(5S)-5-methyl-5-phenylhydantoin in the form of an off-white solid melting at 242°C (Yield = 66%; $[\alpha]_D^{29^\circ} = +113^\circ$ (c = 1.0 in ethanol)).

In the same way, but using (-)-S- α -methylbenzylamine, (-)-(5R)-5-methyl-5-phenylhydantoin is recovered in the form of an off-white solid melting at 248°C (Yield = 54%; $[\alpha]_D^{29^\circ} = +120^\circ$ (c = 1.0 in ethanol)).

In the same way, the following analogous compounds of formula XIIa were obtained:



XIIa

Compound No.	R ⁶	$[\alpha]_D$ (c) Solvent	M.p. (°C)	Yd (%)
35	H	+113° (1.0) EtOH	242	66
36	H	-120° (1.0) EtOH	248	54
37	4-F	+111° (0.8) EtOH	230	44
38	4-F	-114° (0.8) EtOH	230	31
39	4-(4-FPh)O	+54° (0.5) EtOH	190	-
40	4-(4-FPh)O	-57° (0.6) EtOH	189	40

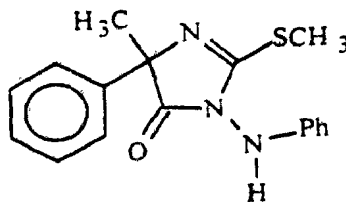
Variant B:

According to a second variant of the process for the preparation of the optical isomers of formula I, the latter are obtained from the corresponding
 5 racemic compounds by high performance liquid chromatography on a chiral stationary phase. A chiral stationary phase of Pirkle type with D-phenylglycine grafts is preferred.

The racemic compounds corresponding to the
 10 formula I are prepared according to the methods described in the three patent applications mentioned in the introduction to the present text.

The examples below illustrate the optically active derivatives of formula I obtained according to
 15 Variant B of the process of preparation.

Example 7: Separation of the (+) and (-) enantiomers of the compound of the following formula (Compounds No. 1 and 2)



The corresponding racemic compound is
 20 prepared according to a procedure analogous to that described in Example 1 of the already mentioned Patent Application EP 551048. This racemic compound is

dissolved in an eluent mixture composed of n-heptane, isopropanol and dichloromethane, in the respective proportion by weight of 93, 5 and 2 %.

2.3 ml of the mixture thus obtained are
5 injected into the chiral, high performance chromatographic column with the following characteristics:

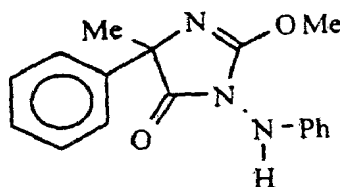
- column of Pirkle type, with a diameter of 10 mm and a length of 250 mm;
- 10 - support: 5 μ m 100 angström silica containing ionic D-phenylglycine grafts.

The flow rate chosen is 10 ml/min and the detector used is a UV detector at 250 nm. The enantiomerically pure compounds are recovered by
15 fractionation and concentration of the pure fractions.

The physical characteristics of the enantiomers obtained, namely the melting point M.p., the optical rotation $[\alpha]_D^{20}$, measured in degrees for the compound dissolved in ethanol at a concentration of 0.5
20 g per 100 ml, and the retention time t_R , have been collated in the table below:

Compound No.	M.p. (°C)	$[\alpha]_D^{20}$	t_R (in minutes)
1	138	+60.7 + or - 1.3	5.73
2	138	-59.6 + or - 0.9	6.55

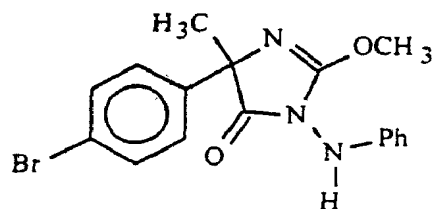
Example 8: Separation of the (+) and (-) enantiomers of the compound of the following formula (Compounds No. 3 and 4):



The corresponding racemic compound is prepared according to a procedure analogous to that described in Example 1 of the already mentioned Patent Application EP 599749. The corresponding (+) and (-) enantiomers (Compounds No. 3 and 4 respectively) are obtained by carrying out the separation in the same way as above. The volume injected into the chiral column is 1.5 ml. The optical rotation is measured after dissolving the compounds in methanol and appears with the other physical characteristics, identical to those determined above, in the table below:

Compound No.	M.p. (°C)	$[\alpha]_D^{20}$	t_R (in minutes)
3	132	+51.3 + or - 1.2	9.89
4	132	-53.2 + or - 1.3	11.17

Example 10: Separation of the (+) and (-) enantiomers of the compound of the following formula (Compounds No. 5 and 6):



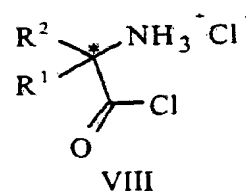
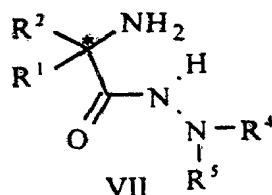
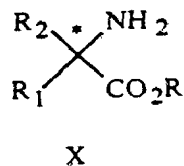
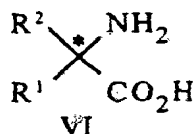
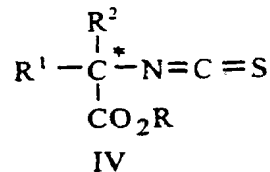
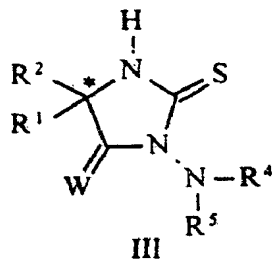
The corresponding racemic compound is prepared according to a procedure analogous to that described in Example 1 of Patent Application EP 599749 already mentioned in the example above. The
 5 corresponding (+) and (-) enantiomers (Compounds No. 5 and 6 respectively) are obtained by carrying out the separation in the same way as above. The results obtained are collated in the table below:

Compound No.	M.p. (°C)	$[\alpha]_D^{20}$ (c)	Solvent	Absolute configuration
5	202	+32.3° (c = 0.5)	MeOH	S
6	202	-32.2° (c = 0.5)	MeOH	R

The absolute configuration of Compounds No. 1 to 4 was determined by chemical correlation with the
 15 absolute configuration of the corresponding α -amino acid described in the literature. The absolute configuration of Compounds No. 5 and 6 was determined by X-ray crystallography.

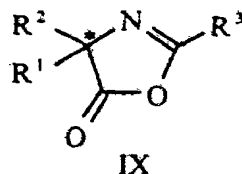
Another subject of the invention is new
 20 optically active compounds useful especially as intermediates in the preparation of the compounds of

formula I. These intermediates have the formulae III, IV, VI, VII, VIII and X:



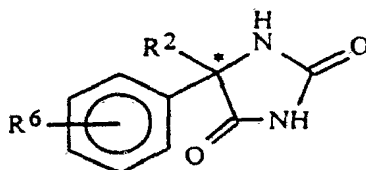
in which R¹ to R⁵ have the same meanings as in the general formula I of the invention,

5 and the compound of formula IX:



in which R¹ and R² have the same meaning as above and R³ represents an optionally halogenated C₁-C₃ alkyl radical,

and the compound of formula XIIb:



XIIb

in which R² has the same meaning as above and R⁶ represents a phenyl, phenoxy or pyridyloxy radical, these radicals optionally being substituted by 1 to 3 groups, which are identical or different, chosen from R⁷ as defined above.

The following examples illustrate the fungicidal properties of Compounds No. 1 to 6, 11 to 14 and 25 to 28 of formula (I) according to the invention.

In these examples, the racemic modification corresponding to enantiomeric Compounds 1 and 2 is recorded as 1+2. Likewise, the racemic modification corresponding to Compounds 3 and 4 is recorded as 3+4. More generally, the racemic modification corresponding to enantiomeric Compounds n and n+1 is recorded as n+(n+1).

Example B1: In vivo test on *Puccinia recondita* (brown rust of wheat):

An aqueous suspension of the active material to be tested is prepared, by fine milling, having the following composition:

- active material: 60 mg
- Tween 80 surface-active agent (oleate of

polycondensate of ethylene oxide with sorbitan) diluted to 10 % in water: 0.3 ml

- volume made up to 60 ml with water.

The active material to be tested is either
5 one of the 2 enantiomers according to the invention or the corresponding racemic modification.

This aqueous suspension is then diluted with water to produce the desired concentration of active material.

10 Wheat of the Talent variety, in pots, sown on a 50/50 peat/pozzolana earth substrate, is treated at the 10 cm high stage by spraying the above aqueous suspension.

After 24 hours, an aqueous suspension of
15 spores ($100,000 \text{ sp/cm}^3$) is sprayed on the wheat; this suspension was obtained from infected seedlings. The wheat is then placed for 24 hours in an incubation cell at approximately 20°C and at 100 % relative humidity, and then for 7 to 14 days at 60 % relative humidity.

20 Monitoring of the condition of the seedlings is carried out between the 8th and 15th day after infection, by comparison with an untreated control. The concentration of active material tested, IC_{75} (expressed in ppm), at which 75 % inhibition of the disease is
25 observed, is then determined.

The results are collated in the following table:

Compound No.	IC ₇₅ (ppm)
1+2	330
1	37
2	>1000
3+4	330
3	110
4	>1000
5+6	330
5	110-330
6	>1000
11+12	37-110
11	12-37
12	-
13+14	37
13	12
14	-
25+26	12
25	-
26	>1000
27+28	37
27	4
28	-

Example B2: In vivo test on *Phytophthora infestans*
(tomato late blight):

An aqueous suspension of the active material

to be tested is prepared, by fine milling, having the following composition:

- active material: 60 mg
- Tween 80 surface-active agent (oleate of polycondensate of ethylene oxide with sorbitan) diluted to 10 % in water: 0.3 ml
- volume made up to 60 ml with water.

The active material to be tested is chosen from the same compounds as in the preceding example.

10 This aqueous suspension is then diluted with water to produce the desired concentration of active material.

Tomato seedlings (Marmande variety) are grown in pots. When these seedlings are one month old (5 to 6-leaf stage, 12 to 15 cm high), they are treated by spraying the above aqueous suspension at various concentrations of the compound to be tested.

After 24 hours, each seedling is infected by spraying with an aqueous suspension of spores (30,000 sp/cm³) of Phytophthora infestans.

After this infecting, the tomato seedlings are incubated for 7 days at approximately 20°C in an atmosphere saturated with moisture.

Seven days after infecting, the results obtained in the case of the seedlings treated with the active material to be tested are compared with those obtained in the case of the seedlings used as controls. The concentration of active material tested, IC₇₅,

(expressed in ppm), at which 75 % inhibition of the disease is observed, is then determined.

The results are collated in the following table:

5		<i>Compound No.</i>	<i>IC₇₅ (ppm)</i>
		1+2	110
		1	37
		2	>1000
		3+4	330
10		3	110
		4	>1000
		5+6	>1000
		5	37
		6	>1000
15		11+12	110
		11	12-37
		12	-
		13+14	110
		13	37
20		14	-
		25+26	110
		25	37
		26	>1000
		27+28	37
25		27	4-12
		28	-

The invention also relates to the compositions for protecting plants against fungal diseases, comprising, in combination with one or more solid or liquid vehicles which are acceptable in agriculture and/or surface-active agents which are also acceptable in agriculture, one (or a number of) active material which is a compound of formula I.

In fact, for their practical use, the compounds according to the invention are rarely used on their own. Most often these compounds form part of compositions. These compositions, which can be used as fungicidal agents, contain, as active material, a compound according to the invention as described above as a mixture with solid or liquid vehicles which are acceptable in agriculture and surface-active agents which are also acceptable in agriculture. In particular, the customary inert vehicles and the customary surface-active agents can be used. These compositions also form part of the invention.

These compositions can also contain all kinds of other ingredients such as, for example, protective colloids, adhesives, thickening agents, thixotropic agents, penetration agents, stabilizing agents, sequestering agents and the like. More generally, the compounds used in the invention can be used in combination with any of the solid or liquid additives which correspond to the usual formulating techniques.

Generally, the compositions according to the

invention usually contain approximately 0.05 to 95 %
(by weight) of a compound according to the invention
(subsequently called active material), one or more
solid or liquid vehicles and, optionally, one or more
5 surface-active agents.

The term "vehicle", in the present account,
means a natural or synthetic, organic or inorganic
material with which the compound is combined in order
to facilitate its application to the plant, to seeds or
10 to the soil. This vehicle is therefore generally inert
and it has to be acceptable in agriculture, especially
to the treated plant. The vehicle can be solid (clays,
natural or synthetic silicates, silica, resins, waxes,
solid fertilizers, and the like) or liquid (water,
15 alcohols, especially butanol, and the like).

The surface-active agent can be an
emulsifying, dispersing or wetting agent of ionic or
nonionic type or a mixture of such surface-active
agents. There may be cited, for example, salts of
20 poly(acrylic acids), salts of lignosulphonic acids,
salts of phenolsulphonic or naphthalenesulphonic acids,
polycondensates of ethylene oxide with fatty alcohols
or fatty acids or fatty amines, substituted phenols
(especially alkylphenols or arylphenols), salts of
25 esters of sulphosuccinic acids, derivatives of taurine
(especially alkyltaurates), phosphoric esters of
polycondensates of ethylene oxide with alcohols or
phenols, esters of fatty acids and of polyols, and the

derivatives of the above compounds having sulphate, sulphonate or phosphate functional groups. The presence of at least one surface-active agent is generally indispensable where the compound and/or the inert
5 vehicle are not soluble in water and where the vector agent of the application is water.

Thus, the compositions for agricultural use according to the invention can contain the active materials according to the invention within very wide
10 limits, ranging from 0.05 % to 95 % (by weight). Their surface-active agent content is advantageously between 5 % and 40 % by weight.

These compositions according to the invention are themselves in fairly diverse, solid or liquid
15 forms.

There may be mentioned, as solid composition forms, powders for dusting (containing the compound at a content of up to 100 %) and granules, especially those obtained by extrusion, by compacting, by
20 impregnation of a granulated vehicle, or by granulation from a powder (the content of the compound in these granules being between 0.5 and 80 % for the latter cases), tablets or effervescent tablets.

The compounds of formula (I) can also be used
25 in the form of powders for dusting; it is also possible to use a composition comprising 50 g of active material and 950 g of talc; it is also possible to use a composition comprising 20 g of active material, 10 g of

finely divided silica and 970 g of talc; these constituents are mixed and milled and the mixture is applied by dusting.

As composition forms which are liquid or
5 intended to constitute liquid compositions during application, there may be mentioned solutions, in particular water-soluble concentrates, emulsifiable concentrates, emulsions, suspension concentrates, aerosols, wettable powders (or sprayable powder),
10 pastes or gels.

The emulsifiable or soluble concentrates most often comprise 10 to 80 % of active material, while the ready-to-apply solutions or emulsions contain 0.001 to 20 % of active material.

15 In addition to the solvent, the emulsifiable concentrates can contain, when this is necessary, 2 to 20 % of suitable additives such as the stabilizing agents, surface-active agents, penetration agents, corrosion inhibitors, dyes or adhesives mentioned
20 above.

It is possible, by diluting these concentrates with water, to obtain emulsions of any desired concentration which are particularly suitable for application to crops.

25 By way of example, the composition of several emulsifiable concentrates will now be given:

EC Example 1

- active material 400 g/l
- alkaline dodecylbenzenesulphonate 24 g/l
- condensate of 10 molecules of ethylene oxide
- 5 with nonylphenol 16 g/l
- cyclohexanone 200 g/l
- aromatic solvent qs 1 litre

According to another emulsifiable concentrate formula, there are used:

10 EC Example 2

- active material 250 g
- epoxidized vegetable oil 25 g
- mixture of alkylarylsulphonate and
of ether of polyglycol and fatty alcohols 100 g
- 15 - dimethylformamide 50 g
- xylene 575 g

The suspension concentrates, which can also be applied by spraying, are prepared so as to produce a stable fluid product which does not settle out and they

20 generally contain from 10 to 75 % of active material, from 0.5 to 15 % of surface-active agents, from 0.1 to 10 % of thixotropic agents, from 0 to 10 % of suitable additives, such as antifoaming agents, corrosion inhibitors, stabilizing agents, penetration agents and

25 adhesives and, as vehicle, water or an organic liquid in which the active material has little or no solubility: certain solid organic materials or inorganic salts can be dissolved in the vehicle to help

in preventing sedimentation or as antifreeze for the water.

By way of example, the composition of a suspension concentrate will now be given:

5 SC Example 1

	- active material	500	g
	- polycondensate of ethylene oxide with tristyrylphenyl phosphate	50	g
10	- polycondensate of ethylene oxide with alkylphenol	50	g
	- sodium polycarboxylate	20	g
	- ethylene glycol	50	g
	- organopolysiloxane oil (antifoam)	1	g
	- polysaccharide	1.5	g
15	- water	316.5	g

The wettable powders (or sprayable powders) are generally prepared so that they contain 20 to 95 % of active material, and they generally contain, in addition to the solid vehicle, from 0 to 30 % of a wetting agent, from 3 to 20 % of a dispersing agent and, when necessary, from 0.1 to 10 % of one or more stabilizing agents and/or other additives, such as penetration agents, adhesives, or anticaking agents, dyes, and the like.

25 In order to obtain the sprayable powders or wettable powders, the active materials are intimately mixed in suitable mixers with the additional substances and the mixture is milled in mills or other suitable

grinders. Sprayable powders are thereby obtained whose wettability and suspensibility are advantageous; they can be suspended in water at any desired concentration and these suspensions can be used very advantageously in particular for application to plant leaves.

Instead of wettable powders, it is possible to produce pastes. The conditions and methods for producing and using these pastes are similar to those for the wettable powders or sprayable powders.

By way of example, various wettable powder (or sprayable powder) compositions will now be given:

WP Example 1

	- active material	50	%
	- condensate of ethylene oxide with fatty alcohol (wetting agent)	2.5	%
	- condensate of ethylene oxide with phenylethylphenol (dispersing agent)	5	%
	- chalk (inert vehicle)	42.5	%

WP Example 2

20	- active material	10	%
	- condensate of 8 to 10 mol of ethylene oxide with C ₁₁ branched-type synthetic oxo alcohol (wetting agent)	0.75	%
	- neutral calcium lignosulphonate (dispersing agent)	12	%
25	- calcium carbonate (inert filler)	qs 100	%

WP Example 3:

This wettable powder contains the same ingredients as in the above example, in the proportions below:

5	- active material	75	%
	- wetting agent	1.50	%
	- dispersing agent	8	%
	- calcium carbonate (inert filler)	qs 100	%

WP Example 4:

10	- active material	90	%
	- condensate of ethylene oxide with fatty alcohol (wetting agent)	4	%
	- condensate of ethylene oxide with phenylethylphenol (dispersing agent)	6	%

15 WP Example 5:

	- active material	50	%
	- mixture of anionic and nonionic surface-active agents (wetting agent)	2.5	%
	- sodium lignosulphonate (dispersing agent)	5	%
20	- kaolin clay (inert vehicle)	42.5	%

The aqueous dispersions and emulsions, for example the compositions obtained by diluting a wettable powder or an emulsifiable concentrate according to the invention using water, are included within the general scope of the present invention. The

emulsions can be of water-in-oil or oil-in-water type and they can have a thick consistency like that of a "mayonnaise".

5 The compounds according to the invention can be formulated in the form of water-dispersible granules also included in the scope of the invention.

10 These dispersible granules, with an apparent density generally between approximately 0.3 and 0.6, have a particle size generally between approximately 150 and 2,000 and preferably between 300 and 1,500 microns.

The active material content of these granules is generally between approximately 1 % and 90 %, and preferably between 25 % and 90 %.

15 The remainder of the granule is essentially composed of a solid filler and optionally of surface-active adjuvants which confer water-dispersibility properties on the granule. These granules can be essentially of two distinct types
20 depending upon whether the filler used is soluble or insoluble in water. When the filler is water-soluble, it can be inorganic or, preferably, organic. Excellent results have been obtained with urea. In the case of an insoluble filler, the latter is preferably inorganic,
25 such as, for example, kaolin or bentonite. It is then advantageously accompanied by surface-active agents (at an amount of 2 to 20 % by weight of the granule) of which more than half consists, for example, of at least

one essentially anionic dispersing agent such as an alkali metal or alkaline-earth metal polynaphthalene sulphonate or an alkali metal or alkaline-earth metal lignosulphonate, the remainder consisting of nonionic
5 or anionic wetting agents such as an alkali metal or alkaline-earth metal alkylnaphthalene sulphonate.

Moreover, although this is not indispensable, it is possible to add other adjuvants such as anti-foaming agents.

10 The granule according to the invention can be prepared by mixing the required ingredients and then granulating according to several techniques known per se (pelletizer, fluid bed, atomizer, extrusion, and the like). Generally, the preparation is completed by
15 crushing followed by sieving to the particle size chosen within the abovementioned limits. It is alternatively possible to use granules obtained as above and then impregnated with a composition containing the active material.

20 Preferably, it is obtained by extrusion, the preparation being carried out as shown in the examples below.

DG Example 1: Dispersible granules

25 90 % by weight of active material and 10 % of urea in the pearl form are mixed in a mixer. The mixture is then milled in a pin mill. A powder is obtained which is moistened with approximately 8 % by weight of water. The damp powder is extruded in a

perforated-cylinder extruder. A granule is obtained which is dried and then crushed and sieved so as to retain only the granules with a size between 150 and 2,000 microns respectively.

5 DG Example 2: Dispersible granules

The following constituents are mixed in a mixer:

- | | | |
|----|--|------|
| | - active material | 75 % |
| 10 | - wetting agent (sodium alkylnaphthalene sulphonate) | 2 % |
| | - dispersing agent (sodium polynaphthalene sulphonate) | 8 % |
| | - water-insoluble inert filler (kaolin) | 15 % |

15 This mixture is granulated in a fluid bed, in the presence of water, and is then dried, crushed and sieved so as to produce granules of between 0.15 and 0.80 mm in size.

20 These granules can be used alone or in solution or dispersion in water so as to produce the required dose. They can also be used to prepare combinations with other active materials, especially fungicides, the latter being in the form of wettable powders or of granules or aqueous suspensions.

25 As regards the compositions which are suitable for storing and transporting, they more advantageously contain from 0.05 to 95 % (by weight) of active substance.

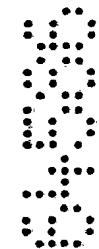
Another subject of the invention is a process

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for the treatment of crops affected by or capable of being affected by fungal diseases, characterized in that an effective amount of an optically active compound of formula I is applied preventively or curatively.

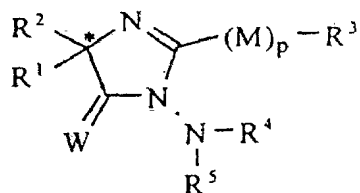
- 5 The compounds of formula I are advantageously applied at doses of 0.005 to 5 kg/ha, and more specifically of 0.01 to 1 kg/ha.

Throughout this specification and claims which follow, unless the context requires otherwise, the word "comprise", or
10 variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated integer or group of integers but not the exclusion of any other integer or group of integers.



THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. Optically active 2-imidazolin-5-one or 2-imidazoline-5-thione derivatives of general formula I,



in which:

- W represents an oxygen or sulphur atom or an S=O group;
- M represents an oxygen or sulphur atom, or an optionally halogenated CH₂ radical;
- p is an integer equal to 0 or 1;
- * means the asymmetric carbon atom corresponding to a stereospecific configuration and that the optically active derivative is substantially free from the other isomer;
- R¹ and R² are different and represent:
 - an alkyl or haloalkyl radical containing 1 to 6 carbon atoms or
 - an alkoxyalkyl, alkylthioalkyl, alkylsulphonylalkyl, monoalkylaminoalkyl, alkenyl or alkynyl radical containing 2 to 6 carbon atoms or
 - a dialkylaminoalkyl or cycloalkyl



radical containing 3 to 7 carbon atoms

or

- an aryl^{or heteroaryl} radical comprising phenyl, naphthyl, thienyl, furyl, pyridyl, benzothienyl, benzofuryl, quinolyl, isoquinolyl or methylenedioxyphenyl, optionally substituted by 1 to 3 groups chosen from R⁶ or

- an arylalkyl, aryloxyalkyl, arylthioalkyl or arylsulphonylalkyl radical, the terms aryl and alkyl having the definitions given above or

- R¹ and R² can form, with the carbon to which they are bonded on the ring, a carbocycle or a heterocycle having from 5 to 7 atoms, it being possible for these rings to be fused to a phenyl, optionally substituted by 1 to 3 groups chosen from R⁶;

- R³ represents:

- a hydrogen or an optionally halogenated C₁-C₃ alkyl radical, when p is equal to 0 or (M)_p is a CH₂ radical,
- an optionally halogenated C₁-C₃ alkyl radical, when (M)_p represents an oxygen or sulphur atom;

-R⁴ represents:

- the hydrogen atom or



5

- an alkyl group containing 1 to 6 carbon atoms or
- an alkoxyalkyl, alkylthioalkyl, haloalkyl, cyanoalkyl, thiocyanatoalkyl, alkenyl or alkynyl group containing 2 to 6 carbon atoms or

10

- a dialkylaminoalkyl, alkoxycarbonylalkyl or N-alkylcarbamoylealkyl group containing 3 to 6 carbon atoms or

15

- an N,N-dialkylcarbamoylealkyl group containing 4 to 8 carbon atoms or
- an ^{or heteroaryl}aryl radical, comprising phenyl, naphthyl, thienyl, furyl, pyridyl, pyrimidinyl, pyridazinyl, pyrazinyl, benzothienyl, benzofuryl, quinolyl, isoquinolyl or methylenedioxyphenyl, optionally substituted by 1 to 3 groups chosen from R⁶ or

20

- an arylalkyl, aryloxyalkyl, arylthioalkyl or arylsulphonylalkyl radical, the terms aryl and alkyl having the definitions given above;

-R⁵ represents:

25

- H, except when R⁴ is H, or
- an alkyl, haloalkyl, alkylsulphonyl or haloalkylsulphonyl radical containing 1 to 6 carbon atoms or



- an alkoxyalkyl, alkylthioalkyl, acyl, alkenyl, alkynyl, haloacyl, alkoxycarbonyl, haloalkoxycarbonyl, alkoxyalkylsulphonyl or
- 5 cyanoalkylsulphonyl radical containing 2 to 6 carbon atoms or
- an alkoxyalkoxycarbonyl, alkylthioalkoxycarbonyl or
- 10 cyanoalkoxycarbonyl radical containing 3 to 6 carbon atoms or
- the formyl radical or
- a cycloalkyl, alkoxyacyl, alkylthioacyl, cyanoacyl, alkenylcarbonyl or alkynylcarbonyl
- 15 radical containing 3 to 6 carbon atoms or
- a cycloalkylcarbonyl radical containing 4 to 8 carbon atoms or
- a phenyl; arylalkylcarbonyl, especially phenylacetyl and
- 20 phenylpropionyl; arylcarbonyl, especially benzoyl, optionally substituted by 1 to 3 groups from R⁶;
- thienylcarbonyl; furylcarbonyl;
- 25 pyridylcarbonyl; benzyloxycarbonyl; furfuryloxycarbonyl;
- tetrahydrofurfuryloxycarbonyl;
- thienylmethoxycarbonyl;

- pyridylmethoxycarbonyl; phenoxycarbonyl
or (phenylthio)carbonyl, the phenyl
being itself optionally substituted by 1
to 3 groups from R⁶; (alkylthio)carbonyl;
5 (haloalkylthio)carbonyl;
(alkoxyalkylthio)carbonyl;
(cyanoalkylthio)carbonyl;
(benzylthio)carbonyl;
(furfurylthio)carbonyl;
10 (tetrahydrofurfurylthio)carbonyl;
(thienylmethylthio)carbonyl;
(pyridylmethylthio)carbonyl or
arylsulphonyl radical or
- a carbamoyl radical, optionally mono-
or disubstituted by:
15 - an alkyl or haloalkyl group
containing 1 to 6 carbon atoms or
- a cycloalkyl, alkenyl or alkynyl
group containing 3 to 6 carbon
20 atoms or
- an alkoxyalkyl, alkylthioalkyl or
cyanoalkyl group containing 2 to 6
carbon atoms or
- a phenyl, optionally substituted
25 by 1 to 3 R⁶ groups;
- a sulphamoyl group, optionally mono-
or disubstituted by:
- an alkyl or haloalkyl group

- containing 1 to 6 carbon atoms or
- a cycloalkyl, alkenyl or alkynyl group containing 3 to 6 carbon atoms or
- 5 - an alkoxyalkyl, alkylthioalkyl or cyanoalkyl group containing 2 to 6 carbon atoms or
- a phenyl, optionally substituted by 1 to 3 R^6 groups;
- 10 - an alkylthioalkylsulphonyl group containing 3 to 8 carbon atoms or a cycloalkylsulphonyl group containing 3 to 7 carbon atoms;
- R^4 and R^5 , taken together, can also form, with the nitrogen atom to which they are attached, a pyrrolidino, piperidino, morpholino or piperazino, optionally substituted by an alkyl containing 1 to 3 carbon atoms, group;
- 15
- 20 - R^6 represents:
- a halogen atom or
 - an alkyl, haloalkyl, alkoxy, haloalkoxy, alkylthio, haloalkylthio or alkylsulphonyl radical containing 1 to 6 carbon atoms or
 - a cycloalkyl, halocycloalkyl, alkenyloxy, alkynyloxy, alkenylthio or alkynylthio radical containing 3 to 6
- 25

carbon atoms or

- the nitro or cyano group or
- an amino radical, optionally mono- or disubstituted by an alkyl or acyl

5 radical containing 1 to 6 carbon atoms
or an alkoxycarbonyl radical containing
2 to 6 carbon atoms

- a phenyl, phenoxy or pyridyloxy
radical, these radicals optionally being
10 substituted by 1 to 3 groups, which are
identical or different, chosen from R^7 ;

- R^7 represents:

- a halogen atom chosen from fluorine,
chlorine, bromine or iodine, or

15 - a linear or branched alkyl radical
containing from 1 to 6 carbon atoms, or

- a linear or branched alkoxy or
alkylthio radical containing from 1 to
6 carbon atoms, or

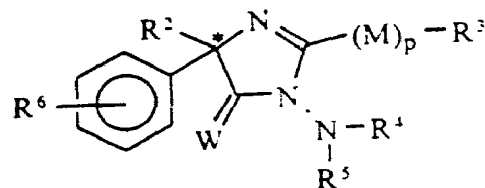
20 - a linear or branched haloalkoxy or
haloalkylthio radical containing from 1
to 6 carbon atoms, or

- a nitrile radical, or

- a nitro radical;

25 and the agriculturally-acceptable salified forms of
these compounds.

2. Optically active compounds according to claim
1 of formula II:

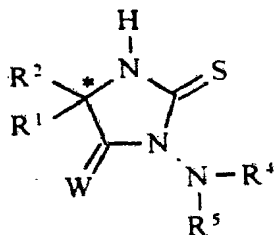


3. Optically active compounds of formula II according to claim 2 in which W represents an oxygen atom.

4. Compound according to claim 3, characterized

5 in that it is the S-(+) enantiomer of the compound of formula II in which W is an oxygen atom, R² is a methyl, M is a sulphur atom, p is equal to 1, R³ is a methyl, R⁴ is a phenyl and R⁵ and R⁶ represent a hydrogen atom.

5. Process for the preparation of the compounds
10 of formula I in which p = 1 and M = S and W = O according to one of claims 1 to 4 by reaction of the compound of formula III:



in which W represents an oxygen atom,

with the compound of formula R³X in which X
15 represents the chlorine, bromine or iodine atom or the

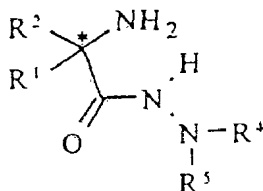
sulphate group or an alkylsulfonyloxy or arylsulfonyloxy group,

in a solvent and in the presence of a base, at a temperature between -5°C and $+80^{\circ}\text{C}$.

- 5 6. Preparation process according to claim 5, characterized in that the solvent is chosen from ethers, cyclic ethers, alkyl esters, acetonitrile, alcohols containing from 1 to 3 carbon atoms or aromatic solvents, preferably tetrahydrofuran.
- 10 7. Preparation process according to claim 5, characterized in that the base is chosen from an alkoxide, preferably potassium tert-butoxide, an alkali metal or alkaline-earth metal hydroxide, an alkali metal carbonate or a tertiary amine.
- 15 8. Process for the preparation of the compounds of formula I in which $p = 1$ and $M = O$ and $W = O$ according to one of claims 1 to 4, characterized in that the corresponding compound of formula I for which $p = 1$ and $M = S$ is reacted with the alcohol of formula
- 20 R^3OH in a solvent, in the presence of a strong base and at a temperature of between 50 and 80°C .
9. Preparation process according to claim 8, characterized in that the strong base is chosen from an alkali metal hydroxide, a strong organic base or an
- 25 alkali metal alkoxide of formula $R^3O^-Met^+$ in which Met^+ represents an alkali metal or alkaline-earth metal.
10. Preparation process according to claim 8, characterized in that the reaction is carried out by

taking the alcohol R^1OH as solvent and the sodium alkoxide $R^1O^-Na^+$ as base.

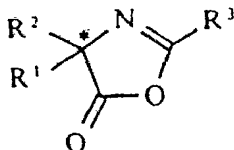
11. Process for the preparation of the compounds of formula I in which $p = 0$ and R^3 is a hydrogen atom according to one of claims 1 to 4 by reaction of the compound of formula VII:



wherein * means the asymmetric carbon atom corresponding to a stereospecific configuration and that the compound is optically active and is substantially free from the other isomer

with an excess of dimethylformamide dimethyl acetal at a temperature between 10 and 100°C.

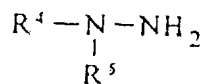
12. Process for the preparation of the optically active compounds of formula I in which R^3 is an optionally halogenated C_1-C_2 alkyl radical and in which $p = 0$ or $p = 1$ and $M = CH_2$ according to one of claims 1 to 3 by reaction of the compound of formula IX:



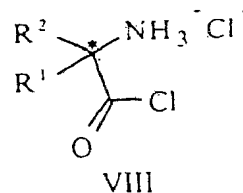
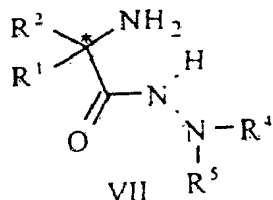
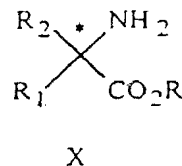
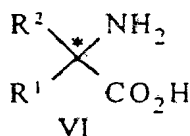
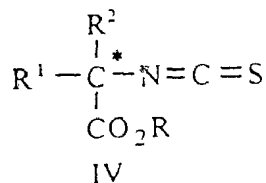
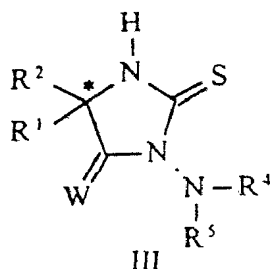
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wherein * means the asymmetric carbon atom corresponding to a stereospecific configuration and that the compound is optically active and is substantially free from the other isomer

with the compound of formula V:



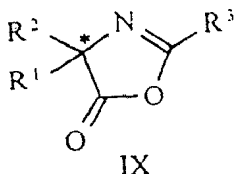
13. Optically active compounds which are useful especially as intermediates in the preparation of the compounds of formula I according to one of claims 1 to 4, characterized in that they have the formula:



in which R represents a C₁-C₄ alkyl wherein * means the asymmetric carbon atom corresponding to a stereospecific configuration and that the optionally active compound is substantially free from the other isomer, and R¹ to R⁵ have the same meanings as in the general formula I of the invention,

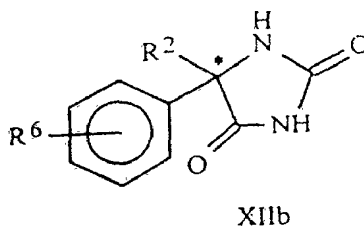
and of formula IX:





in which * has the same meaning as above, R³ represents an optionally halogenated C₁-C₃ alkyl radical,

and of formula XIIb:



in which * has the same meaning as above, R² has the same meaning as above and

5 R⁶ represents a phenyl, phenoxy or pyridyloxy radical, these radicals optionally being substituted by 1 to 3 groups, which are identical or different, chosen from R⁷ as defined above.

14. Compounds according to claim 13,
10 characterized in that, in the formulae III, IV, VI, VII, VIII and IX, R¹ is a phenyl and R² is a methyl.

15. Fungicidal compositions comprising, in combination with one or more solid or liquid vehicles which are acceptable in agriculture and/or surface-active agents which are also acceptable in agriculture,
15 one (or a number of) active material chosen from the compounds of formula I according to one of claims 1 to



4.

16. Process for the treatment of crops affected by or capable of being affected by fungal diseases, characterized in that an effective amount of an

5 optically active compound of formula I according to one of claims 1 to 4 is applied preventively or curatively.

17. Process for the treatment of crops according to claim 16, characterized in that the compounds of formula I are applied at doses of 0.005 to 5 kg/ha, preferably of 0.01 to 1 kg/ha.

10

18. Optically active compounds according to claim 1, processes for the preparation thereof, or fungicidal compositions comprising said compounds, or processes for the use thereof, substantially as hereinbefore described with reference to the Examples.

~~19. The steps, features, compositions and compounds disclosed herein or referred to or indicated in the specification and/or claims of this application, individually or collectively, and any and all combinations of any two or more of said steps or features.~~

DATED this SEVENTH day of JUNE 1994

Rhone-Poulenc Agrochimie

by DAVIES COLLISON CAVE

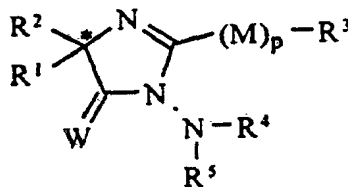
Patent Attorneys for the applicant(s)



ABSTRACT

Fungicidal optically active 2-imidazolin-5-one and 2-imidazoline-5-thione derivatives

1. Optically active 2-imidazolin-5-one and 2-imidazoline-5-thione derivatives.
2. They are of general formula I:



with

$M = O, S$ or optionally halogenated CH_2

$W = O, S$ or $S=O$

$p = 0$ or 1

R^1, R^2 and R^4 are a hydrocarbon, especially aryl, radical which is optionally substituted, especially by halogen atoms

R^3 is H or optionally halogenated C_1 - C_2 alkyl

R^5 is a hydrocarbon radical.

3. Use as agricultural fungicides.